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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/673,667

09/30/2003

Gregory D. Sempowski

1579-861

2031

23117

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EXAMINER

XIE, XIAOZHEN

ART UNIT

PAPER NUMBER

1646

MAIL DATE

DELIVERY MODE

06/01/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/673,667

Applicant(s)

SEMPOWSKI ET AL.

Examiner

Xiaozhen Xie

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 February 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1 and 4-19 is/are pending in the application.
- 4a) Of the above claim(s) 6-9 and 13-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,4,5,10-12 and 16-19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>20070228, 20070308</u>  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Response to Amendment***

The Information Disclosure Statements (IDS) filed on 28 February 2007 and 8 March 2007 have been entered. Applicant's amendment of the claims filed on 28 February 2007 is acknowledged.

Claims 2 and 3 are cancelled. Claims 16-19 have been added. Claims 1 and 4-19 are pending. Claims 6-9 and 13-15 are withdrawn from further consideration as being drawn to a nonelected invention. Claims 1, 4, 5, 10-12 and 16-19 are under examination in this office action.

### ***Claim Objections/Rejections Withdrawn***

The objection to claim 1 for informalities is withdrawn in response to Applicant's amendment of the claim.

The rejection of claims 1-5 and 10-12 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in response to Applicant's amendment of the claims to limit an anti-LIF antibody or fragment thereof.

The rejection of claims 1-5 and 10-12 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement, is withdrawn in response to Applicant's amendment of the claims to limit an anti-LIF antibody or fragment thereof, and to remove the word "preventing" in the preamble phrase.

The rejection of claim 10 under 35 U.S.C. § 112, second paragraph, for the recitation of "said antagonist" which lacks antecedent basis, is withdrawn in response to Applicant's amendment of the claim.

The rejection of claims 1-5, 10 and 12 under 35 U.S.C. 103(a) as being unpatentable over Wang et al., in view of Jansen et al., and further in view of Watanobe et al., is withdrawn in response to Applicant's amendment of claim 1 to recite administering an anti-LIF antibody or fragment thereof.

### ***New Grounds of Rejections***

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. §112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 11 recite "said treatment or prevention". There is insufficient antecedent basis for the limitation.

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 5, 10-12 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Haynes et al. (WO 00/62805, International Publication Date: 26 October 2000).

The claims are directed to a method of treating gram-negative endotoxin-induced thymic atrophy, comprising administering an anti-LIF antibody or fragment thereof that inhibits LIF induction of thymic corticosteroids sufficient to effect said treatment (claims 1, 16), wherein the antibody or fragment thereof inhibits intracellular or membrane-associated events that occurs between LIF and a LIF receptor, or inhibits interaction between LIF and a LIF receptor (claims 4, 5), wherein the antibody or fragment thereof is administered directly to the thymus (claim 10), wherein the method further comprises administering a compound that promotes thymic activation or growth (claim 11), wherein the patient is a human (claim 12).

WO 00/62805 teaches a method of reversing or treating thymic atrophy comprising administering to a patient, e.g., a human, in need thereof an antagonist of the overproduced cytokine, and/or administering an agonist of the under-produced cytokine (pp. 9, lines 2-7, and pp. 10, lines 19 through pp. 11, line 3.). WO 00/62805 teaches that the antagonist includes antibodies to the overproduced cytokine, such as LIF (pp. 11, line 4-10, and pp. 10, line 5-7). The binding of LIF to the antibody would inherently interfere with the interaction between LIF and a LIF receptor, and inhibits membrane-associated events that occur between them. WO 00/62805 teaches that corticosteroids mediate LIF-induced thymic atrophy, and lipopolysacchride (LPS) (a gram-negative endotoxin) induces the LIF induction (see Example 4, pp. 23, lines 4-6,

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pp. 24, lines 9-15, pp. 25, lines 7-13). WO 00/62805 teaches that the antagonist can be administered directly to the thymus to minimize systemic side effect (pp. 11, lines 20-22). Therefore, WO 00/62805 anticipates the instant claims.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/62805, in view of Kim (U. S. Patent No: 6,544,749 B1, which has a priority filing on 8 May 1992).

WO 00/62805 teaches as set forth above. WO 00/62805, however, does not teach that the anti-LIF antibody is a monoclonal, humanized or chimeric antibody, and that the fragment thereof is a Fab or F(ab')<sub>2</sub> fragment (claims 17-19).

The '749 patent teaches anti-LIF antibodies that include monoclonal, humanized and chimeric antibodies, and antibody fragments, for example, Fab, F(ab')<sub>2</sub> and Fv fragments (column 1, lines 19-23, column 3, lines 54-60, column 5, lines 40-43).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of WO 00/62805, with those of the '749 patent to treat Gram-negative endotoxin-induced thymic atrophy in a human patient by administering an anti-LIF antibody, such as a monoclonal, humanized or

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chimeric antibody, or a fragment thereof, such as a Fab or F(ab')<sub>2</sub> fragment to the patient. One of ordinary skill in the art would have been motivated to combine the teachings, because WO 00/62805 teaches treating thymic atrophy induced by LPS of Gram-negative bacteria by administering an anti-LIF antibody, the '749 patent teaches different forms of the antibodies and fragments. Therefore, the combined teachings provide a reasonable expectation of successfully treating Gram-negative endotoxin-induced thymic atrophy in a patient.

### ***Conclusion***

**NO CLAIM IS ALLOWED.**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

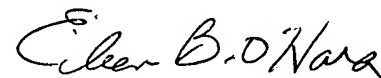
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D.  
May 17, 2007



EILEEN B. O'HARA  
PRIMARY EXAMINER